

REMARKS/ARGUMENTS

With this amendment, claims 1-5, 21-22, 59, and 61 are pending. Claims 5 and 60 are cancelled. For convenience, the Examiner's rejections are addressed in the order presented in an October 8, 2004 Office Action.

I. Status of the claims

Claims 1 and 59 are amended to recite that at least 80% of the terminal galactose residues present on the glycoprotein are sialylated. Support for this amendment is found throughout the specification, for example, at page 3, lines 1-3 and at page 10, lines 5-7. These amendments add no new matter.

Claim 4 is amended to remove the word substantially. This amendment adds no new matter.

Claim 21 is amended to more clearly state that the sialyltransferase is an ST3Gal I enzyme. This amendment adds no new matter and is not a limiting amendment.

II. Amendments to the specification

The Office Action requests updating of the relationship of the present application to its parent application, which has issued as a US Patent. Applicants have amended the specification to comply with this request.

III. Sequence listing

The Office Action requests that a sequence listing be filed to identify a sequence found on page 3 of the specification. Applicants have submitted a separate communication under 37 CFR §§1.821-1.825 with an amendment, a computer readable sequence listing, and a paper copy of the sequence listing.

IV. Rejections under 35 U.S.C. §112, second paragraph

Claim 4 is rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite from recitation of the word "substantially." In order to expedite prosecution, Applicants have amended claim 4 to remove the word "substantially."

Claim 5 is rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite. In order to expedite prosecution, claim 5 is now canceled.

Claim 21 is rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite from recitation of the phrase "recombinant expression of a sialyltransferase in a host cell." In order to expedite prosecution, Applicants have amended claim 21 to more clearly state that the sialyltransferase is an ST3Gal I enzyme.

Claim 59 is rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite from recitation of the phrase "a greater percentage of terminal galactose residues are sialylated. . ." In order to expedite prosecution, Applicants have amended claim 59 to recite that at least 80% of the terminal galactose residues present on the glycoprotein are sialylated.

In view of the above amendments and remarks, withdrawal of the rejection under 35 U.S.C. §112, second paragraph is respectfully requested.

V. Rejections under 35 U.S.C. §112, first paragraph, enablement

Claim 5 is rejected under 35 U.S.C. §112, first paragraph because the specification allegedly fails to comply with enablement requirement. In order to expedite prosecution, Applicants have canceled claim 5.

VI. Rejections under 35 U.S.C. §102(b)

Claims 1-2, 5, 21, and 59-61 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Williams *et al.*, *Glyconjugate J.* 12:755-761 (1995). To the extent the rejection applies to the amended claims, Applicants respectfully traverse.

To anticipate a claim, the reference must teach every element of the claim. "A claim is anticipated only if each and every element as set forth in the claim is found...in a single prior art reference." *Verdegaal Bros. v. Union Oil of California*, 814 F.2d 628, 631, 2 USPQ2d

1051, 1053 (Fed. Cir. 1987). Thus, in order to anticipate, the cited references must contain every element of the claims at issue.

The amended claims now recite that the commercial-scale production method of sialylating a saccharide group on a recombinant glycoprotein using an ST3Gal I protein results in sialylation of at least 80% of the terminal galactose residues present on the glycoprotein. Although the Office Action asserts that Williams *et al.* teach at least 80-90% sialylation of terminal saccharide residues on a glycoprotein using an ST3Gal I protein, this interpretation of the reference is not correct.

As evidence, Applicants submit as Exhibit A a copy of a declaration signed by Dr. James Paulson and first submitted in the parent application; USSN 09/007,741, now US Patent No. 6,399,336. Dr. Paulson states that Williams *et al.* do not disclose a method of sialylation that is identical to the claimed methods and do not disclose quantitation of or 80-90% sialylation of terminal saccharide residues on a glycoprotein. Thus, the cited reference does not disclose all the elements of the claimed invention.

In view of the above amendments and remarks, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §102(b).

VII. Rejections under 35 U.S.C. §103(a)

Claims 3, 4, and 22 are rejected under 35 U.S.C. §103(a) as allegedly obvious over Williams *et al.* in view of Wong *et al.*, US Patent No. 5,374,541; Kurosawa *et al.*, BBA 1244:216-222 (1995); and Paulson *et al.* US Patent No. 5,541,083. To the extent the rejection applies to the amended claims, Applicants respectfully traverse.

The Office Action has not established a case of *prima facie* obviousness. To establish a case of *prima facie* obviousness, the Examiner must meet three basic criteria:

First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim

limitations. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). M.P.E.P. §§ 706.02(j) and 2143.

The references cited by the Examiner fail to provide a reasonable expectation of success in practicing the invention and fail to provide a motivation for the combination of the references. In addition, the references cited by the Examiner fail to provide all the elements of the rejected claims.

According to 35 U.S.C. §103(a), A claimed invention is unpatentable if the differences between it and the prior art "are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art." The phrase "at the time the invention was made" ensures that obviousness analysis is performed without the benefit of impermissible hindsight. The Federal Circuit has ruled that

... the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references. . . . Combining prior art references without evidence of such a suggestion, teaching, or motivation simply takes the inventor's disclosure as a blueprint for piecing together the prior art to defeat patentability--the essence of hindsight. *In re Dembicza*k, 50 USPQ2d 1614, 1617 (1999), citations omitted.

The Federal Circuit recognizes that evidence of a suggestion, teaching or motivation to combine can be found in a number of sources. However, actual evidence of a suggestion, or teaching, or motivation to combine is required and the showing of a suggestion, or teaching, or motivation to combine must be "clear and particular." *Id.*

The Office Action alleges again that Williams *et al.* teach a method of sialylating at least 80-90% of terminal saccharide residues on a glycoprotein using an ST3Gal I protein. In addition, the Office Action alleges that Wong *et al.* teach a method of in situ regeneration of CMP-sialic acid, that Kurosawa *et al.* teach a recombinant ST3Gal I enzyme that can be used in the claimed methods, and that Paulson *et al.* methods of making recombinant sialyltransferases without membrane spanning domains. Office Action at page 10-11.

As argued above in view of a declaration from Dr. James Paulson, Williams *et al.* do not disclose quantitation of or 80-90% sialylation of terminal saccharide residues on a glycoprotein. The other cited references, *i.e.*, Kurosawa *et al.*, Wong *et al.*, and Paulson *et al.*, do not remedy this deficiency of Williams *et al.* In particular, Kurosawa *et al.* do not quantify sialylation of a glycoprotein by an ST3Gal I protein and do not disclose 80-90% sialylation of terminal saccharide residues on a glycoprotein. Thus, the combination of cited references does not disclose all the elements of the claimed invention.

Moreover, Williams *et al.* teach away from use of recombinant ST3Gal I for commercial-scale production of glycosylated recombinant proteins. Williams *et al.* disclose that recombinant ST3Gal I had a specific activity of 3.1 U/mg, *i.e.*, three-fold lower than the 10.6 U/mg value reported for the native enzyme purified from porcine submaxillary glands. Thus, one of skill would not have had motivation to combine the cited references to arrive at the claimed methods. Moreover, even if the cited references were combined, one of skill would not have had a reasonable expectation of success in arriving at the claimed invention because of the requirements for commercial scale production of glycosylated recombinant proteins with at least 80% sialylation of galactose residues.

In view of the above amendments and remarks, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §10(a).

VIII. Rejections for non-statutory double patenting

In response to the obviousness-type double patenting rejection over claims in the parent patent (US Patent 6,399,336), Applicants will file an appropriate terminal disclaimer, once the outstanding rejections are resolved.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Appl. No. 10/081,456
Amdt. dated March 8, 2005
Reply to Office Action of October 8, 2004

PATENT

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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Attachments

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